

The University of Chicago

THE PINACOL-PINACOLONE MOLECULAR
REARRANGEMENT: THE REARRANGEMENT
OF 2-PHENYLAMINOTETRAMETHYL
ETHANOL

A PART OF A DISSERTATION SUBMITTED TO
THE FACULTY OF THE DIVISION OF THE
PHYSICAL SCIENCES IN CANDIDACY FOR
THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

1933

By
PAUL VERNON BROWER

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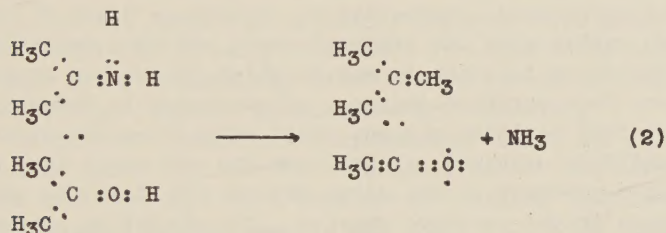
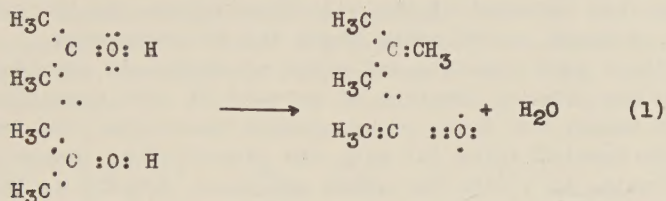
The author desires to express his appreciation to Professor Julius Stieglitz for the assignment of this interesting research, and for guidance and encouragement throughout the work. The author is also greatly indebted to Dr. R. W. Johnson and Dr. K. H. Adams for many helpful suggestions and discussions.



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I. INTRODUCTION

The similarity of the pinacol-pinacolone and amino alcohol rearrangements is illustrated by the following reactions for tetramethyl pinacol and 2-aminotetramethyl ethanol:



These rearrangements are instances of the application of a principle enunciated by W. Ostwald, to the effect that compounds in intermediate stages of oxidation of an element quite generally tend, by inter- or intramolecular oxidation and reduction reactions, to change into the ultimate reduction and the highest oxidation forms of the element. A simple illustration of the principle is the transformation of hypochlorites into chlorides and chlorates and perchlorates. Stieglitz and his collaborators¹ have

¹References to the earlier work, carried on since 1893, are found in articles by Stieglitz and Leach, *J. Am. Ch. Soc.*, 36, 272 (1914) and Stieglitz and Stanger, *ibid.*, 38, 2046 (1916). For the Theory of the pinacol-pinacolone rearrangement and investigations growing out of this theory see doctorate dissertations (University of Chicago) of:

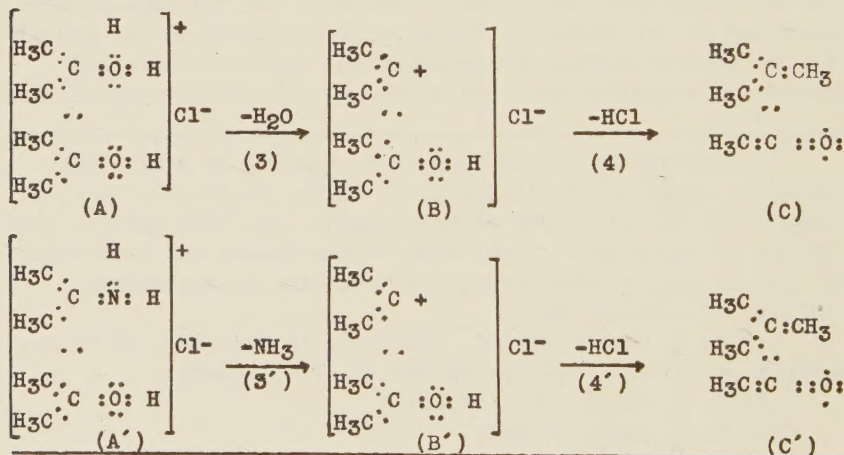
(a) R. B. Cooper (1930), published in Abstracts of Theses, University of Chicago, Science Series, 8, 77 (1929-30).

(b) G. W. Ayers, Jr. (1931).

(c) K. H. Adams (1932).

studied molecular rearrangements from this point of view,² with the particular object of determining the path by which the release, and the necessary shifts, of electrons and radicals carried by them could be effected. The two partially oxidized carbinol, or amino and carbinol, carbon atoms in a pinacol or amino alcohol evidently do not represent a condition of maximum stability; but the compounds are rather stable in themselves and their valence electrons are clearly under rather stable constraints. Only an attack, in its ultimate nature electrical in character, which would make possible the free movement of the valence electrons of the carbon atoms in question, could bring about the rearrangement.

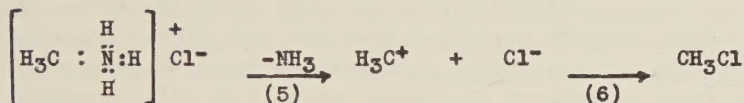
Since both pinacols and amino alcohols are rearranged by acids and the primary function of an acid is salt formation, the Stieglitz theory for their rearrangement postulates that the acids first form oxonium salts (A) with the pinacols and substituted ammonium salts (A') with the amino alcohols, exactly as they do with ordinary alcohols and amines. The cations of the salts then lose water or ammonia, respectively, (reactions 3 and 3') with an ease which varies with the compound used; and thus unstable intermediate carbonium ions are formed in which the carbon atoms involved have free positive charges, as expressed in formulas B and B'. These free positive charges would attract nearby electrons and the radicals attached to them, and the way would thus be opened for the free movement of the alkyl groups :CH₃ from the neighboring carbon atoms to the positive charges. The migration of the groups :CH₃ to the exposed positive charges of the carbonium ions comprises the actual molecular rearrangement. Finally the hydrogen on the remaining hydroxyl group ionizes (reactions 4 and 4') and the rearrangement is complete. The following equations express these changes:



²Cf. also L. W. Jones, Am. Chem. J., 50, 440 (1913).

In the final product, pinacolone, it will be noted that the one carbon atom has been completely reduced and the second, the ketonic carbon atom has moved in the direction of complete oxidation. Thus, the rearrangement represents an instance of the application of Ostwald's principle.

The course of these reactions, up to the point of rearrangement, is the ordinary course of the action of a strong acid on alcohols and amines, especially under the influence of heat. Thus, methyl amine and hydrochloric acid form methylammonium chloride, which when heated breaks down into methyl chloride and ammonia; in this decomposition, no doubt a methyl group and ammonia are first formed and the chloride ion combines with the methyl ion to form methyl chloride:



Similarly, in the formation of methyl chloride from methyl alcohol and hydrochloric acid, an oxonium salt is undoubtedly first formed, which loses water, especially under the influence of heat, and by the union of H_3C^+ and Cl^- produces methyl chloride.

It is well known that alkylammonium salts are more stable than oxonium salts and that the decomposition of the alkylammonium chlorides usually requires a considerably higher temperature for their decomposition into ammonia and alkyl chlorides than is required for the formation of alkyl chlorides from alcohols. In agreement with this general relation we find it necessary to work at temperatures of the order of 175° for the study of the molecular rearrangement of 2-aminotetramethyl ethanol, whereas the rearrangement of pinacol itself is conveniently studied at 100° .

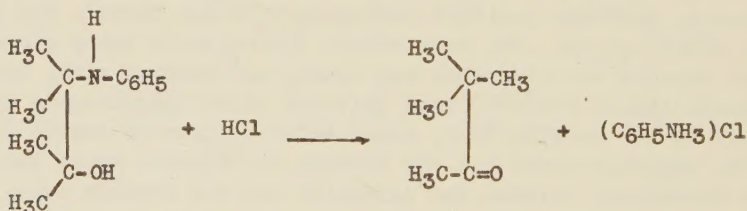
In the rearrangement reactions, according to the Stieglitz theory, when the positive carbonium ions are formed, the capture of methyl groups $:\text{CH}_3$ from within the molecule takes place before the outside chloride ions can reach, and combine with, the carbonium ions. Ayers^{1b} found that the solid hydrobromide of pinacol, that is the oxonium salt, loses water readily to form a bromide (the bromohydrine); but the bromide in solution where the solvent is interposed between the carbonium and the bromide ions, is rearranged.

Salt formation is an ionic reaction, hence is instantaneous. Likewise, the final rearrangement of the unstable intermediate ion must be a very fast reaction since otherwise a chloride would be formed. Thus, the speed of the rearrangement is limited by the rate of dehydration of the oxonium ion, or the deamination of the substituted ammonium ion.

Further, the salts of all very weakly basic amino alcohols and pinacols are highly hydrolyzed; hence the concentrations of the oxonium and substituted ammonium cations, and the rates of rearrangement dependent thereon, are approximately proportional to the acid concentrations. On the other hand, the salts of all strongly basic amino alcohols are very slightly hydrolyzed; therefore the concentrations of the substituted ammonium cations and the rates of rearrangement should be proportional to the acid concentration only up to the point of complete salt formation.

In agreement with expectations, it has been found by Cooper^{1a} that the rate of rearrangement at 100° of the weakly basic tetramethyl pinacol, whose salts are almost completely hydrolyzed, bears a linear relationship to the acid concentrations. On the other hand, Adams^{1c} has found that the rate of rearrangement at 175° of the strongly basic 2-aminotetramethyl ethanol or pinacol amine shows a tendency to become constant at acid concentrations above that for complete salt formation. However, this amino alcohol did show a considerable increase in the rate of rearrangement with excess acid concentrations. This was attributed to a supplementary tendency of the tertiary alcohol group to react through the formation of an oxonium salt and the loss of water and thus promote a parallel rearrangement.³

These results indicated that a more weakly basic 2-amino alcohol, such as 2-phenylaminotetramethyl ethanol, $(\text{CH}_3)_2\text{C}(\text{NHC}_6\text{H}_5)\text{C}(\text{OH})(\text{CH}_3)_2$, should show a lesser tendency for salt formation and hence the relation between the rate of rearrangement and acid concentration should be of a nature intermediate between those of tetramethyl pinacol and of 2-aminotetramethyl ethanol. It was anticipated that 2-phenylaminotetramethyl ethanol would rearrange in acid solutions to give aniline and pinacolone:



In order to test these predictions, the writer, at the suggestion of Professor Stieglitz, undertook the preparation of 2-phenylaminotetramethyl ethanol and a study of its rearrangement.

³For details see K. H. Adams, loc.cit.

II. DISCUSSION OF RESULTS

2-Phenylaminotetramethyl ethanol, $(\text{CH}_3)_2\text{C}(\text{NHC}_6\text{H}_5)\text{C}(\text{OH})(\text{CH}_3)_2$, was prepared from pinacol oxide and sodium anilide in aniline solution and purified by distillation. Details of the procedure used will be found in the Experimental Part.

2-Phenylaminotetramethyl ethanol was found to require an equivalent of four molecules (or eight atoms) of bromine for its bromination to one molecule of tribromoaniline and two molecules of acetone. On the other hand, aniline, a rearrangement product of 2-phenylaminotetramethyl ethanol, requires an equivalent of only three molecules of bromine for its bromination to tribromoaniline. This difference in the behavior of the two amines was used to determine the extent of the rearrangement of 2-phenylaminotetramethyl ethanol.

It was expected that 2-phenylaminotetramethyl ethanol would rearrange more easily, that is at lower temperatures and faster, than 2-aminotetramethyl ethanol because aniline is a weaker base than is ammonia, hence the hold of the phenylamino group on the carbon atom, an alkyl carbon atom. would be decidedly weaker than that of the amino group. This was found to be decidedly the case; thus, 2-aminotetramethyl ethanol hydrochloride (0.1000 M) must be heated 82 hours at 175° for a 49 per cent rearrangement, whereas 2-phenylaminotetramethyl ethanol hydrochloride (0.1000 M) was 40 per cent rearranged in 10 hours at 130° (see Table II and Adams^{1a}, p. 51).

The course of the rearrangement of 2-phenylaminotetramethyl ethanol was determined from the products of the reaction of an aqueous solution of the hydrochloride (0.1000 M) heated at 130° for 42 hours. The solution smelled very strongly of pinacolone. The pinacolone semicarbazone was readily formed and accounted for 90 per cent of the pinacolone corresponding to complete rearrangement. The iodoform test for acetone was negative; it gave only the cloudy solution formed with pinacolone. Bromination analyses indicated that 96.5 per cent rearrangement had taken place. The foregoing results prove that 2-phenylaminotetramethyl ethanol in the presence of acids rearranges to pinacolone and aniline. Determinations of the rate of rearrangement showed the reaction to be monomolecular. The constancy of the values obtained for the velocity coefficients indicated the absence of side reactions, such as the formation of 2,3-tetramethyl indolene, $\text{C}_6\text{H}_4.\text{C}(\text{CH}_3)_2.\text{C}(\text{CH}_3)_2\text{NH}$, through ring

closure by condensation of the pinacol hydroxyl group at the ortho position of the phenyl group.

Anhydrous 2-phenylaminotetramethyl ethanol did not undergo a pinacol rearrangement when heated at 175° for 74 hours. Not a trace of the odor of pinacolone could be detected. On the other hand, Nessler's reagent gave a precipitate with the reaction mixture, whereas it does not react with 2-phenylaminotetramethyl ethanol. This result would indicate that rearrangement or some other change had taken place. However, we have found that Nessler's reagent gives precipitates with traces of unknown substances sometimes formed when pinacol derivatives are heated. No pinacolone semicarbazone could be obtained. This indicated the absence of appreciable quantities of pinacolone. The iodoform test for acetone gave slightly more than the usual cloudiness obtained with pinacolone, which was considered negative for both pinacolone and acetone. The writer considers the very characteristic odor of pinacolone to be the most sensitive and reliable test for traces of the compound in mixtures with odorless substances such as those encountered in the rearrangement of 2-phenylaminotetramethyl ethanol.

It is possible that simple pyrolysis of 2-phenylaminotetramethyl ethanol at 175° could give acetone and isopropyl aniline. Bromination showed that some kind of a change had taken place. Calculated as rearrangement this change would amount to 9.1 per cent in 28 hours, and 15.2 per cent in 74 hours. However, the total absence of the odor of either acetone or pinacolone and the negative iodoform and semicarbazone tests indicates that some other change had taken place; possibly formation of 2,3-tetramethyl indolene, $C_6H_4.C(CH_3)_2.C(CH_3)_2NH$, or N-diphenyl-2,3,5,6-octamethyl piperazine, $C_6H_5N.C.C(CH_3)_2.C(CH_3)_2.N(C_6H_5).C(CH_3)_2.C(CH_3)_2$, occurred.

At 175° the rearrangement of 2-phenylaminotetramethyl ethanol takes place in pure water in the course of 49 hours. A pronounced odor of pinacolone could be detected in this test. Pinacolone was further identified by the preparation of its semicarbazone. Bromination indicated 54.4 per cent of rearrangement. Another test heated 25 hours rearranged to the extent of 54.2 per cent. This apparent discrepancy in the degrees of rearrangement is apparently due to the fact that 2-phenylaminotetramethyl ethanol is insoluble in water at room temperatures but somewhat more soluble at higher temperatures. The sample that rearranged the more rapidly was the smaller; the amount of water was the same in both tests. The limited solubility of the amino alcohol in water made the determination of authentic rate constants impossible under these conditions.

TABLE I
THE REARRANGEMENT OF 2-PHENYLAMINOTETRAMETHYL ETHANOL
IN AQUEOUS HYDROCHLORIC ACID SOLUTIONS

Temperature	Concentration of the amine (moles per liter)	Concentration of H Cl (moles per liter)	K Rate of rear- rangement per mole per hour
130	0.02500	0.02500	0.0712
130	0.05000	0.05000	0.0695
130*	0.1000	0.1000	0.0722
130	0.1500	0.1500	0.0720
130	0.1000	0.5000	0.0830
130	0.1000	1.000	0.0871
130	0.02500	0.2500	0.0913
125	0.1000	0.1000	0.0413
125	0.1000	1.000	0.0492
135	0.1000	0.1000	0.122

*These data from experimental results of Table II.

The rate of rearrangement of 2-phenylaminotetramethyl ethanol hydrochloride was found to be independent of its concentration over a range of 0.02500 to 0.1500 M (Table I). This proved the reaction to be monomolecular. It is also additional proof of our theory that the rate of rearrangement is limited by the rate of the deamination of the cation of 2-phenylaminotetramethyl ethanol hydrochloride. Similar results were obtained by Adams^{1c} for 2-aminotetramethyl ethanol hydrochloride.

The strength of 2-phenylaminotetramethyl ethanol as a base was determined from the hydrogen ion concentration of solutions of the hydrochloride, as measured by the hydrogen electrode method. The ionization constant was found to be $K_I = 2.70 \times 10^{-8}$. Thus, 2-phenylaminotetramethyl ethanol is about one hundred times as strong a base as is aniline, due to the strong base producing characteristics of the pinacol group. 2-Phenylaminotetramethyl ethanol is so strong a base, as a result of the predominating influence of the pinacol group over the phenyl group, that in a 0.1000 M solution of its hydrochloride only 0.02 per cent of the salt is dissociated into the free base and free acid. Thus, complete suppression of the hydrolysis of the salt by means of an excess of an acid could cause an increase in the rate or rearrangement of only 0.02 per cent. Larger increases, ranging from 15 to 20 per cent, were observed when five to ten times the equivalent of hydrochloric acid was used in excess.

The rate of rearrangement of a solution of 0.1000 M 2-phenylaminotetramethyl ethanol in 0.5000 M hydrochloric acid showed a rate increase of 15.0 per cent as compared to the rate for a 0.1000 M solution of the hydrochloride in which there was an absence of an excess of acid. For a solution of 0.1000 M amine in 1.000 M hydrochloric acid the corresponding rate increase was 20.6 per cent. These results indicate that acid concentrations higher than 1 M would cause only a small further increase in the rate of rearrangement of the hydrochloride.

The addition of an excess of acid to two different dilutions of 2-phenylaminotetramethyl ethanol hydrochloride had almost the same effect upon the rate of rearrangement. The rates of reaction differed by 20.6 per cent in the case of a 0.1000 M solution of the hydrochloride compared to a solution of 0.1000 M amine in 1.000 M hydrochloric acid. Similarly, the rates of reaction for a 0.02500 M solution of the hydrochloride and a 0.02500 M solution of the amine in 0.2500 M hydrochloric acid differed by 28.2 per cent. In either combination, the ratio of acid to amine was ten fold that required for complete formation of the hydrochloride. The more pronounced effect of the addition of acid to the lower dilution of the amine could not have been due entirely to suppression of the degree of hydrolysis because the hydrolysis of the hydrochloride in 0.01000 M solution was found to be only 0.6 per cent and would have been still less in a 0.02500 M solution of the hydrochloride. It seems, therefore, more probable that the greater increase in rate of rearrangement afforded by addition of an excess of acid to the lower dilution of the amine hydrochloride was probably due to the greater activity of the acid in the more dilute solutions. In any event, the rate of rearrangement did not increase with the total ionic strength as would probably be predicted by Brönstead's theory of acid and base catalysis.⁴

The increase in the rate of rearrangement of 2-phenylaminotetramethyl ethanol hydrochloride caused by excess acid must be due to a supplementary tendency of the alcohol group to facilitate rearrangement (see p. 4). The increase of 20.6 per cent found for a ten fold increase in acid concentration, is very small compared to the increase of 860 per cent observed by Adams^{1c} in the case the rearrangement of 2-aminotetramethyl ethanol at 175° under otherwise similar conditions. It is evident that the lower temperature of rearrangement of 2-phenylaminotetramethyl ethanol hydrochloride, greatly reduces the influence of the alcohol group.

⁴See K. H. Adams^{1c}, loc.cit. Also "Symposium on the Kinetics of Homogeneous Reactions," Chem. Rev., 10, Feb., 1932; Brönstead, Z. physik. Chem., 102, 169 (1922); 115, 337 (1925); Chem. Rev., 3, 191 (1931); Ibid., 5, 231 (1928).

The effect of temperature upon the rate of rearrangement of 2-phenylaminotetramethyl ethanol is as follows (based upon data from Table I):

0.1000 M amine in
0.1000 M HCl.

$$\frac{K_{130}}{K_{125}} = 1.76$$

$$\frac{K_{135}}{K_{130}} = 1.69$$

$$\frac{K_{135}}{K_{125}} = 2.96$$

0.1000 M amine in
1.000 M HCl

$$\frac{K_{130}}{K_{125}} = 1.77$$

It will be noted that most of these ratios are for 5° intervals instead of the usual 10° interval. These results show that the effect of temperature upon the rates of rearrangement of 2-phenylaminotetramethyl ethanol is almost the same as observed by Adams^{1c} for 2-aminotetramethyl ethanol (3.0 and 3.4 at 10° intervals).

III. EXPERIMENTAL PART

1. Consideration of Methods for the Preparation of 2-Phenylaminotetramethyl Ethanol.- A simple method for the preparation of a 2-amino ethanol was used by Rindfusy and Harnack⁵ who prepared β -hydroxyethyl aniline by refluxing aniline and ethylene chlorohydrine in the presence of sodium carbonate for 3 to 4 hours. We were unable to obtain suitable conditions for a similar reaction between aniline and pinacol chlorohydrine; refluxing these substances for 27 hours in the presence of sodium carbonate gave no 2-phenylaminotetramethyl ethanol that could be detected by the Hinsberg⁶ benzenesulfonyl chloride test for secondary amines. However, the method was not tested conclusively because in the meantime other results had been obtained which indicated that difficulties might be encountered. For instance, it was found that traces of pinacol chlorohydrine and aniline reacted to give 2,3-tetramethyl indolene $C_6H_4.C(CH_3)_2.C(CH_3)_2.NH$ even in the presence of sodium anilide. The boiling points of 2,3-tetramethyl indolene and 2-phenylaminotetramethyl ethanol are only 10° apart, both compounds⁷ are secondary amines, and their basic strengths seem to be almost the same, which factors make the separation of the two compounds virtually impossible.

The reaction of aniline with pinacol oxide gave poor yields of 2,3-tetramethyl indolene and N-diphenyl-2,3,5,6-octamethyl piperazine,⁸ $C_6H_5N.C(CH_3)_2.C(CH_3)_2.NC_6H_5.C(CH_3)_2.C(CH_3)_2$. It is possible that the formation of these products was catalyzed by small amounts of pinacol chlorohydrine present in the pinacol oxide.

The reaction of pinacol chlorohydrine and sodium anilide was so violent that the chlorohydrine was rearranged to pinacolone. An attempt was made to moderate the reaction by dilution of the chlorohydrine with solvents such as ligroin, ether and benzene; extreme dilution or cooling simply prevented the occurrence of any reaction.

⁵Rindfusy and Harnack, J. Am. Chem. Soc., 42, 1720 (1920).

⁶Hinsberg and Kessler, Ber., 38, 907 (1905); Vaubel, "Quantitative Bestimmung Organischer Verbindungen," Vol. II, p.160.

⁷See later sections for the preparation and properties of these compounds.

⁸Ibid.

This result suggested that the use of sodium anilide and pinacol oxide instead of pinacol chlorohydrine, would give a less violent reaction and thus prevent rearrangement. This method would also prevent the formation of any tertiary amine and at the same time would totally block any ring closure that might result in the formation of 2,3-tetramethyl indolene. This scheme gave the desired 2-phenylaminotetramethyl ethanol in a 30 per cent yield.

The pinacol oxide used in this method was prepared from pinacol chlorohydrine which was in turn prepared from anhydrous pinacol.

2. The Preparation of Anhydrous Pinacol.- Pinacol was prepared by the reduction of acetone by means of magnesium and mercuric chloride.⁹ Satisfactory results were obtained only with the best grade of magnesium turnings. Double quantities were used in the preparation and the reaction was carried out in a 12 liter flask. This method gave pinacol hexahydrate which was dehydrated under reduced pressure according to the method of K. H. Adams.^{1c} We found that further purification of the pinacol by distillation could best be accomplished at reduced pressure instead of at atmospheric pressure. There was usually some impurity in the pinacol which seemed to catalyze its decomposition in the neighborhood of its boiling point (172°) at atmospheric pressure. The final distillation was carried out in a Claissen flask (1 liter) with a capillary air tube to prevent bumping. The last traces of water from the dehydrated crude pinacol soon distilled over, whereupon the temperature rose to 89-92° at a pressure of 15 mm. The boiling point as a rule fluctuated within this temperature range due to pressure changes. It was usually possible to recover 35-50 gm. more of anhydrous pinacol by recrystallization of the impure distillates. This was added to the main part of the yield and gave a total yield of 315 gms. of pure pinacol.

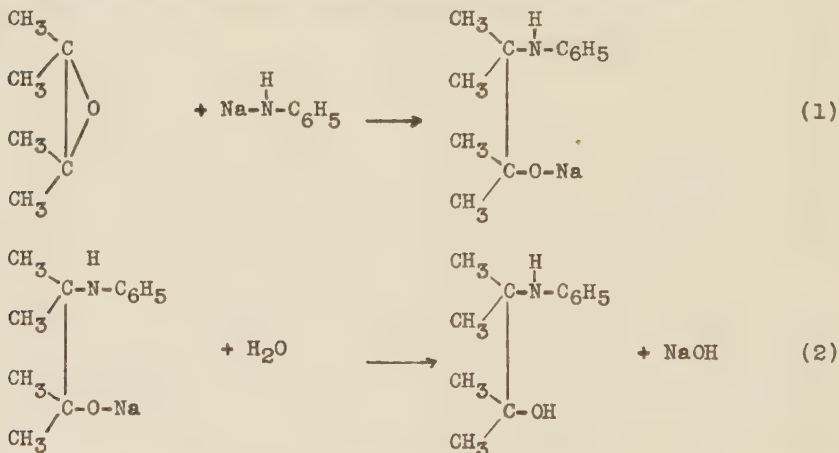
3. The Preparation of Pinacol Chlorohydrine and Pinacol Oxide.- Pinacol chlorohydrine was prepared according to the method of Delacree,¹⁰ which is based upon the reaction of anhydrous pinacol with dry hydrogen chloride at 40-45°. The technique followed was essentially that of Adams^{1c} and Ayers.^{1b} The yield of unre-crystallized chlorohydrine varied from 72-82 per cent of the theory.

⁹Roger Adams, "Organic Synthesis," (John Wiley and Sons, New York, 1925, Vol. V., p. 87.

¹⁰Delacree, Bull. soc. chim., 4, 3, 203 (1908); 4, 1, 586 (1907); Bayer and Co., P.D.R. 317, 635 (1916); Chem. Centr. (1920) II, 445.

Pinacol oxide was prepared from pinacol chlorohydrine by treatment with concentrated ammonium hydroxide. Pinacol chlorohydrine (134 gms.) was allowed to stand over night with concentrated ammonium hydroxide (150 c.c.). The best results were obtained when the reaction was not allowed to become warm; this was prevented by means of a water bath kept at room temperature. The next day ammonia gas was passed into the reaction mixture for 14 hours about as rapidly as it could be absorbed. The reaction mixture was motor stirred during this period. At the end of this stage of the reaction, the oxide layer was separated and dried over night over stick potassium hydroxide. This crude oxide was slowly distilled over stick potassium hydroxide until the temperature reached 95°, whereupon the potassium hydroxide was removed to prevent decomposition of the residue. The 90-95° distillate contained most of the oxide. The residue was further distilled and the 90-95° fractions were added to the first distillate. Further fractionation of this product did not seem greatly to improve its purity as indicated by its boiling range. The yield was 68 gms. or 70 per cent of the theoretical.

4. The Preparation of 2-Phenylaminotetramethyl Ethanol.-The preparation of 2-phenylaminotetramethyl ethanol from pinacol oxide and sodium anilide involves the following reactions:



The sodium anilide was prepared by the reaction of aniline and sodium amide.¹¹ The amount of sodium amide used (14.6 gms.) corresponded to an excess of 25 per cent based upon the pinacol oxide (30.0 gms). The lumps of sodium amide were ground to a powder

¹¹Titherley, J. Chem. Soc., (Trans.) 71, 46 (1898); Ibid. 65, 504 (1894).

under ether. The powder and ether were transferred to a 500 c.c. three-necked flask. One side opening was connected to a potassium hydroxide drying tower and a cylinder of nitrogen. A dropping funnel and rubber stopper were in the center opening. A water cooled condenser was connected to the other side outlet.

The aniline used was distilled over potassium hydroxide and zinc dust and was almost water white. The amount of aniline used (35.0 gms.) corresponded to an excess of 10 per cent based on the sodium amide. This excess aniline served as a solvent for the solid sodium anilide and thus assured complete reaction of the latter with pinacol oxide in a subsequent step of the preparation. The slow addition of aniline to the sodium amide was accompanied by a vigorous evolution of ammonia. At the end of about 15 minutes all of the aniline had been added and practically all of the ether had evaporated with the ammonia. The contents of the flask were slowly heated in an oil bath until at the end of 45 minutes the bath temperature had reached 160°. The temperature was maintained at 160-175° for ten minutes, and during this interval the nitrogen tube was closed by a pinch clamp and the remaining ammonia removed from the reaction mixture by means of a slight suction afforded by the water pump. The outlet tube was closed with a pinch clamp and the reaction flask quickly brought up to atmospheric pressure by admission of nitrogen. The cooled reaction mixture was a brownish black, and viscous solution of sodium anilide in aniline.

The pinacol oxide was added to the sodium anilide solution and the mixture heated on a water bath for 6 to 8 hours. This operation was carried out in an atmosphere of dry nitrogen. The reactants were stirred by a motor. During this period of reaction mixture reached a maximum viscosity. The product contained sodium 2-phenylaminotetramethyl ethanolate formed according to reaction (1). Without the excess aniline as a solvent, the reaction took place very slowly if at all.

It was found that traces of pinacol chlorohydrine in the pinacol oxide gave a final product low in oxygen and carbon and high in nitrogen as compared to pure 2-phenylaminotetramethyl ethanol. This was no doubt due to the presence of 2,3-tetramethyl indolene formed as a result of the reaction of aniline and the traces of pinacol chlorohydrine. Pinacol oxide prepared by the reaction of ammonia and pinacol chlorohydrine always gave unsatisfactory results unless it was slowly distilled from solid potassium hydroxide.

The solution of sodium 2-phenylaminotetramethyl ethanolate was cooled in an atmosphere of nitrogen. It was then hydrolyzed by the slow addition of water (50 c.c.) without stirring. The temperature was kept at that of the room by means of a water bath.

At the end of 1 1/2 hours, hydrolysis was complete. The product contained 2-phenylaminotetramethyl ethanol formed according to reaction (2).

The separation of the water and amine layers was facilitated by addition of 50 c.c. of ether. The ether layer was dried several hours with stick potassium hydroxide as traces of water caused frothing during subsequent distillation. Any sediment present at the end of this operation was removed by filtration. The ether was evaporated and the amine transferred to a modified Claissen flask with a short distillation column and condenser attached. The amine mixture was distilled under a pressure of not more than 10 mm. Distillation at a higher pressure (162-163° at 15 mm.) gave an abnormally dark product which was thought to be the result of a slight decomposition. Excessive bumping was prevented by use of a half dozen ebullition tubes long enough to extend up beyond the side neck of the flask. At 7 mm. pressure any pinacolone, pinacol oxide, and most of the aniline had come over by the time the temperature had reached 120°. The temperature then rose sharply to 142°. The fraction boiling at 140-145° was saved. The product so obtained usually contained at least two impurities insoluble in dilute hydrochloric acid; one was a sweetish smelling substance and the other was an orange colored crystalline solid; their boiling points seemed to be very close to that of 2-phenylaminotetramethyl ethanol which prevented purification by fractional distillation.

These impurities were removed by treatment of the product with the exact amount of 1 N hydrochloric acid calculated to form 2-phenylaminotetramethyl ethanol hydrochloride. The acid insoluble impurities were extracted with two successive portions of ether (50 c.c. each). The amine was precipitated from the hydrochloric acid solution with 50 c.c. of 20 per cent sodium hydroxide and the amine extracted with 50 c.c. of ether. This process removed the orange colored solid and the sweetish smelling substance; neither was identified.

In one preparation, another impurity was encountered which as compared to 2-phenylaminotetramethyl ethanol, was more strongly basic and contained a higher percentage of nitrogen and a lower percentage of carbon. This impurity was not identified but was probably 2-aminotetramethyl ethanol. Its removal was easily accomplished by treatment of the preceding ether solution with 5 per cent of the hydrochloric acid (1 N) calculated to form 2-phenylaminotetramethyl ethanol hydrochloride. The ether layer was removed and neutralized with 50 c.c. of 20 per cent sodium hydroxide, and then dried with potassium hydroxide sticks for several hours. The product was redistilled to assure complete removal of ether

and aniline and to remove a slight discoloration, usually brown or green. The product was water white and boiled sharply at 142°, at 7 mm. of mercury. The yield was about 30 per cent of the theoretical based upon the pinacol oxide. The amine was slightly hygroscopic, hence was kept in a desiccator over potassium hydroxide sticks.

The most satisfactory test of the purity of the different batches of 2-phenylaminotetramethyl ethanol was the analysis for the carbon content which was carried out by micro-combustions (Pregel).

5. Properties and Proof of the Structure of 2-Phenylaminotetramethyl Ethanol, $(CH_3)_2C(NHC_6H_5)C(OH)(CH_3)_2$.- 2-Phenylaminotetramethyl ethanol has not been previously reported in the literature. It is a colorless and odorless oil (b.p. 142° at 7 mm.), insoluble in water but soluble in dilute hydrochloric acid. It reacts as a secondary amine in the Hinsberg benzenesulfonyl chloride test. The determination of the molecular weight, and micro-combustion analyses for carbon, hydrogen and nitrogen, proved the identity of the compound:

Analyses (Pregel) of three preparations gave:

Preparation	1		2		3		Theory
C (%)	74.47	74.37	74.45	74.66	74.56	74.57	74.55
H (%)	9.99	10.07	9.84	9.87	9.86	10.02	9.92
N (%)	7.06	7.21	7.34	7.17			7.25

The molecular weight (cryoscopic in benzene) was found to be 214; the theoretical is 193.16.

6. 2-Phenylaminotetramethyl Ethanol Hydrochloride, $(CH_3)_2C(OH).(NH_2C_6H_5)(CH_3)_2 Cl^-$.- The hydrochloride of 2-phenylaminotetramethyl ethanol was precipitated from ether with dry hydrogen chloride. The precipitation did not take place in benzene solution. The precipitate was crystalline and was obtained much more readily than was aniline hydrochloride. The hydrochloride was washed with dry benzene and dried by suction with a rubber diaphragm over the funnel to prevent access of air and moisture. The product was kept overnight in a desiccator over concentrated sulfuric acid to remove benzene. It was then left overnight in a desiccator over lime to remove any free acid. Another preparation differed in the fact that desiccation with sulfuric acid and lime covered a period of a week each. Both preparations gave almost identical hydrogen ion concentrations in aqueous solutions as determined by the hydrogen electrode. Aniline hydrochloride prepared

in exactly the same manner gave a hydrogen ion concentration in aqueous solution in good agreement with the best experimental values.

2-Phenylaminotetramethyl ethanol hydrochloride melts and decomposes with complete volatilization sharply within the range, 185.5 to 186.0° u.c. or 187.0 to 187.5° corr.

Analysis: Calc. for $C_{12}H_{20}ONCl$, Cl, 15.50; found Cl, 15.52.

7. The Ionization Constant of 2-Phenylaminotetramethyl Ethanol.— The ionization constant of 2-phenylaminotetramethyl ethanol was calculated from the hydrogen ion concentrations of solutions of the hydrochloride:

$$K_I = \frac{C \times 10^{-14}}{[H^+]^2}$$

Where C = concentration of amine hydrochloride the degree of hydrolysis = $\frac{[H^+]}{C}$. The method is based upon the degree of hydrolysis of the salt.

The hydrogen ion concentrations of the chloride solutions were determined by means of a cell composed of a hydrogen electrode and a saturated calomel electrode connected by means of a bridge of saturated potassium chloride. A solution of known concentration of the amine hydrochloride was placed in the hydrogen electrode beaker. The E.M.F. of the cell was measured by means of a standard potentiometer. A similar method has been used by Krantz and Hartung¹² for a number of amino alcohols.

The hydrogen electrode was made from a platinum wire. To clean the electrode, it was boiled in aqua regia and electrolyzed in 10 per cent hydrochloric acid and then in 10 per cent sulfuric acid. The platinum black was plated from a 3 per cent solution of chloroplatinic acid to which had been added 2 drops of 0.025 M lead acetate per 25 c.c. of solution.

The saturated calomel electrode was used because of its ruggedness and reliability.¹³ The electrode was standardized as assembled by means of a half-cell composed of a hydrogen electrode bathed by a 0.05000 N solution of potassium acid phthalate the standard electrode potential of which¹⁴ is 0.2310 volts at 20°. The potential of the entire cell was found to be 0.472 volt, therefore the potential of the calomel half cell was 0.241 volts. The same value was found when the calomel cell was standardized against a quinhydrone electrode bathed by the phthalate solution.

¹²Krantz and Hartung, J. Am. Phar. Assoc., 19, 461 (1930).

¹³Clark, "The Determination of Hydrogen Ions," Williams and Wilkins Co., 1928, pp. 314 and 486.

¹⁴Hall and Spinkel, J. Am. Ch. Soc., 54, 3472 (1932).

All calculations were made by means of the following equation:

$$E_{\text{obs}} = 0.241 + \frac{1.9885 T}{23,074} \log \frac{1}{(H^+)}$$

Measurements were made for 2-phenylaminotetramethyl ethanol hydrochloride and for aniline hydrochloride, prepared as described in section 6, page 15. The hydrogen ion concentrations were roughly checked by means of standard tubes of p-bromophenol blue indicator. The solution temperature in all measurements was 19°.

	E.M.F. (Milli- volts)	(H) ⁺ x 10 ⁵	K _I x 10 ⁸	pH Hydrogen Electrode	pH Indicator
0.01000 M 2-phenylaminotet- ramethyl ethanol hydrochloride. (Prep. 1).	0.485	6.18	2.61	4.2	4.2
0.01000 M 2-phenylaminotet- ramethyl ethanol hydrochloride. (Prep. 2).	0.487	5.71	3.07	4.2	4.2
0.1000 M 2-phenylaminotet- ramethyl ethanol hydrochloride. (Prep. 2).	0.455	2.04	2.42	3.7	3.8
Average			2.70		
0.01 M aniline hydrochloride	0.437	41.6	0.0459	3.4	3.0

The value found for aniline (4.59×10^{-10} at 19°) is in good agreement with an average value from the literature¹⁵ (4.62×10^{-10} at 25°).

¹⁵Stewart, J. Chem. Soc., 87, 410 (1905); Ibid., 87, 185 (1905).

8. Methods of Analysis for the Determination of the Rate of Rearrangement of 2-Phenylaminotetramethyl Ethanol.- A suitable method of analysis for the determination of the speed of rearrangement of 2-phenylaminotetramethyl ethanol must afford a means for the estimation of either the concentration of the original 2-phenylaminotetramethyl ethanol or of one of the products of rearrangement, aniline or pinacolone.

In the present work it was at first hoped that it would be possible to estimate both the original 2-phenylaminotetramethyl ethanol and the aniline formed in the rearrangement, with the aid of the Hinsberg¹⁶ benzenesulfonyl chloride method for the separation of primary and secondary amines. However, it was found that the dibenzenesulfonyl derivative of aniline¹⁷ is also formed in considerable quantities, and, since its hydrolysis back to the monosulfonyl derivative of aniline promised to be a complicated and unreliable process, the method was abandoned.

In the bromination of 2-phenylaminotetramethyl ethanol, it was found that eight bromine atoms are involved in the reaction instead of the six anticipated on the basis of the presence of a single anilido group. On the other hand, in the bromination of aniline, the normal six bromine atoms enter into the reaction, tribromoaniline being formed. This difference suggested that the reaction could be used to determine the proportions of aniline and 2-phenylaminotetramethyl ethanol in their mixtures, and that the method could be used to study the rate of rearrangement of the latter.

The bromination of 2-phenylaminotetramethyl ethanol was carried out under conditions identical with those used in the bromination of aniline.¹⁸ For example: A solution of 2-phenylaminotetramethyl ethanol (10.00 c.c. of 0.1000 M) was diluted with 100 c.c. of water and 25 c.c. of 10 per cent potassium bromide was added to the solution. Then enough 0.2000 N potassium bromate was added to give an estimated excess corresponding to 4 to 8 c.c. of 0.1000 N sodium thiosulfate. In the bromination of a rearrangement mixture the procedure was the same except less potassium bromate was used, but approximately the same excess was added in all cases.

¹⁶Hinsberg and Kessler, Ber., 38, 907 (1905); Vaubel, "Quantitative Bestimmung Organischer Verbindungen," Vol. II, p.60.

¹⁷Salonia, Zentr., 1899, II, 867; J. Russ. Phys. Chem., 31, 640-55.

¹⁸Curme, Doctorate Dissertation, University of Chicago, 1913; Callahan and Henderson, J. Chem. Ind., 41T, 161.

Finally 5 c.c. of concentrated hydrochloric acid was added. The loss of free bromine from the flask was prevented by a drying tube filled with glass beads moistened with potassium iodide. All of the excess iodide was shaken from the tube lest some of it drip into the bromination mixture and destroy the small excess of potassium bromate. Twenty minutes was allowed for bromination at room temperature. During this period the contents of the flask were frequently shaken. Next, 10 c.c. of a 10 per cent potassium iodide solution was added through the glass beads and the contents of the flask were vigorously shaken to assure contact of bromine vapors with the iodide. Ten minutes were allowed for completion of this reaction. The liberated iodine was titrated with standard sodium thiosulfate and starch indicator.

In these titrations the end point did not reach a constant value for about 30 minutes in the analyses for pure 2-phenylaminotetramethyl ethanol, and in the case of the more highly rearranged mixtures a period of 2 hours sometimes elapsed before reliable values were obtained. Sodium thiosulfate was added at half hour intervals, until a point was reached where there was no appreciable color change during a half hour; this was taken as the final end point. The reason for the shifting end point was not determined but it is probable that it was due to traces of 2,3-tetramethyl indolene, because in analyses for this compound by bromination only fairly reliable end points were reached after 24 hours. Pure aniline did not give a sluggish end point. It was possible to determine pure aniline or pure 2-phenylaminotetramethyl ethanol with an accuracy of 0.25 to 0.50 per cent in 10.00 c.c. 0.1500 to 0.02500 M solutions of the amines. The accuracy was somewhat less than this in the case of the rearrangement mixtures due to the greater shift of the end point.

The yellow precipitate formed in the bromination of 2-phenylaminotetramethyl ethanol was recovered on a filter. Upon recrystallization from alcohol, colorless needles were obtained which melted at 120.5 u.c. The melting point of tribromoaniline¹⁹ is 119-120°. The acetyl derivative of the recrystallized precipitate was prepared by heating with acetyl chloride. The melting point of the product recrystallized from alcohol was found to be 232° u.c. as compared to 232° for tribromoacetanilide.²⁰

¹⁹Remmers Ber. 7, 349 (1874); Mulliken, "Identification of Pure Organic Compounds," J. Wiley and Sons, 1922, Vol. IV, pp. 147, 152.

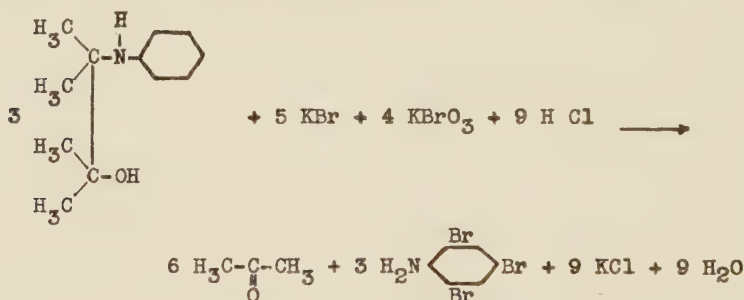
²⁰Ibid.

The precipitates from several bromination experiments were dried over potassium hydroxide for 48 hours and weighed:

Sample of 10.00 c.c. of 0.1000 M original amine	1	2	3	Theory
Weight found	0.3179 g.	0.3302 g.	0.3230 g.	0.3298 g.

These results show that the recovery of tribromoacetanilide was close to 100 per cent of that represented by the theory.

The filtrates from the tribromoaniline precipitates gave strong tests for a ketone with Nessler's reagent and with phenylhydrazine. This ketone could not be pinacolone because it had been found that the action of bromine on 2-phenylaminotetramethyl ethanol involved an oxidation of the pinacol part of the molecule to an extent corresponding to the reduction of two bromine atoms to bromide ions, whereas pinacolone is formed by intramolecular oxidation and reduction of pinacol and its amino derivatives and is not itself an oxidation product requiring an outside oxidizing agent for its formation. Pinacolone is not brominated under the conditions of the experiments. The only reaction that could agree with these facts seemed to involve the formation of acetone, as follows:



Acetone is not brominated under the conditions of the experiments.

The filtrates from three bromination tests of 2-phenylaminotetramethyl ethanol were combined and two-thirds of the solution distilled in order to separate any volatile organic products of the bromination reaction from the inorganic products. This distillate was redistilled and the first 54 c.c. of the second distillate was distilled to give a third distillate. The first 2 c.c. of the third distillate gave a heavy precipitate on treatment with benzaldehyde in alkaline solution. The precipitate recrystallized

from alcohol melted at 110-111° u.c. as compared to 110-111° for dibenzylidene acetone.²¹ The presence of acetone was thus demonstrated.

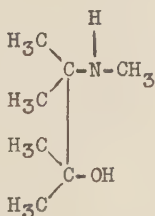
The acetone content of the first distillate (two-thirds distilled) of the filtrate of a bromination analysis was determined quantitatively by means of the iodoform reaction.²²

Sample	Na ₂ S ₂ O ₃ (0.1004 N) (c.c.)	I ₂ (0.3016 N) (c.c.)	Moles acetone per mole of amine
From 10.00 c.c. 0.1000 M amine	41.50	50.00	1.8
From 10.00 c.c. 0.1000 M amine	50.92	55.00	1.9

The accuracy of the iodoform analysis was found to be about 5 per cent. These analyses showed the acetone content to correspond to 1.8 and 1.9 molecules of acetone per molecule of 2-phenylaminotetramethyl ethanol.

The foregoing study conclusively proves that the reaction follows the course depicted above. The products of the bromination of 2-phenylaminotetramethyl ethanol are additional proof of its structure.

An interpretation of the course of the reaction is of interest. It is obvious that the molecule is severed at two points upon bromination. On the other hand, 2-methylaminotetramethyl ethanol,²³



gave no apparent reaction when it was subject to the bromination test under conditions identical to those used for the bromination

²¹Mulliken, "Identification of Pure Organic Compounds," Wiley and Sons, New York, 1904, Vol. I, p. 146.

²²Mathews, "Physiological Chemistry," W. Wood and Co., New York, 1916, 2nd Ed. p. 1006.

²³This compound was prepared by Dr. K. H. Adams from pinacol oxide and methylamine by reaction in a bomb at 100° for 36 hours. One volume of oxide was used with about 5 volumes of a 25 per cent solution of the methyl amine.

of aniline and 2-phenylaminotetramethyl ethanol. From these facts we can deduce that in the bromination of 2-phenylaminotetramethyl ethanol, the phenyl group is the first to be brominated. The tribromoaniline group so formed apparently weakens the bond with the carbon atom of the pinacol group and causes the rupture of this bond. Oxidation by bromine follows, two molecules of acetone being formed.

9. The Rearrangement of 2-Phenylaminotetramethyl Ethanol.-

The rearrangement tests were carried out according to the method used by K. H. Adams.^{1c} The entire contents of each rearrangement bomb tube were brominated. The rates of rearrangement were determined from the bromination analyses by plotting experimental values of $\log \frac{1}{c'}$ against the time, where c' , is the fraction of the amine not rearranged. An average curve was then drawn through the points. Next, average values of $\log \frac{1}{c}$ were read from the average curve. The corresponding zero time, O_2 , for these values was usually taken as 2 hours from the actual zero time when a tube was lowered into the thermostat. The actual zero points could not be used because the rearrangements did not start until the tubes reached the reaction temperature. Furthermore, the zero points as taken, were average values from the average experimental curves; consequently, they were more accurate than any single experimental point could be. Finally, the velocity constants were calculated from the following equation:

$$K = \frac{2.303}{t} \left(\log \frac{1}{c_t} - \log \frac{1}{c_0} \right)$$

where t is the time in hours and $\log \frac{1}{c_t}$ corresponds to a given time, t , read from the zero time, O_2 . $\log \frac{1}{c_0}$ is read at the zero time, O_2 . A sample table of the experimental and calculated data obtained for one set of conditions is given in Table II.

TABLE II

REARRANGEMENT OF 2-PHENYLAMINOTETRAMETHYL ETHANOL
(0.1000 M) IN HCl (0.1000 M) AT 130°

Preparation 2			
Time (Hours)	KBrO ₃ (0.2000 N) (c.c.)	Na ₂ S ₂ O ₃ (0.09970) (c.c.)	Fraction Not Rearranged
2	42.00	6.95	0.802
3	41.00	7.28	0.738
4	40.50	7.65	0.669
5	40.00	6.91	0.656
7, 42	39.00	6.87	0.558
10	37.50	6.29	0.437
14	37.50	7.60	0.372
18	36.00	6.95	0.254
23	35.00	6.75	0.164

Preparation 3			
8	38.58	6.20	0.551
12.50	37.00	5.77	0.365
15.50	36.50	6.59	0.323
19	35.50	6.48	0.226
21	35.00	5.67	0.217

Data Calculated from Average Experimental Curve

Time (Hours)	Log $\frac{1}{c}$	K
0.2	0.090	
1	0.120	0.0691
2	0.152	0.0714
4	0.215	0.0720
6	0.278	0.0722
9	0.371	0.0719
13	0.497	0.0721
17	0.639	0.0744
22	0.797	0.0741
Average 0.0722		

VI. THE PREPARATION AND PROPERTIES OF 2,3-TETRAMETHYL INDOLENE,
 $\text{C}_6\text{H}_4 \cdot \text{C}(\text{CH}_3)_2 \cdot \text{C}(\text{CH}_3)_2 \cdot \text{NH}$, AND THE POSSIBLE FORMATION OF
 N-DIPHENYL-2,3,5,6-OCTAMETHYL PIPERAZINE,
 $\text{C}_6\text{H}_5 \cdot \text{N} \cdot \text{C}(\text{CH}_3)_2 \cdot \text{C}(\text{CH}_3)_2 \cdot \text{N} \cdot \text{C}_6\text{H}_5 \cdot \text{C}(\text{CH}_3)_2 \cdot \text{C}(\text{CH}_3)_2$

The fact that the reaction between aniline and pinacol chlorohydrine to give 2,3-tetramethyl indolene seemed to take place so easily, suggested the possibility of the formation of this compound through a condensation of the hydroxyl group of 2-phenylaminotetramethyl ethanol at the ortho position of the phenyl group, under the conditions of rearrangement of the latter. Therefore, the indolene was prepared in the pure state and a study made of its properties.

Pinacol chlorohydrine (30 gms.) was heated with twice the theoretical amount of aniline (41 gms.) in a bomb at 125 to 130° for 27 hours. The amine was purified in the same manner as the 2-phenylaminotetramethyl ethanol (see pp. 14-15). The product was a water white oil and had a slightly sweetish odor. It boils at 132° under a pressure of 7 mm. The yield was 10.5 gms. or 27 per cent of the theoretical. No attempt was made to improve the yield.

A portion of the product was redistilled and the middle fraction identified by combustion analysis (Pregel). Calc. for $\text{C}_{12}\text{H}_{17}\text{N}$, C, 82.23; H, 9.76; N, 7.99. Found: C, 82.23, 82.03; H, 9.85, 9.76; N, 8.13, 7.99. The molecular weight (cryoscopic benzene) was 164 as compared to the theoretical 175.14.

Bromination analyses of 2,3-tetramethyl indolene were carried out in the same manner as for 2-phenylaminotetramethyl ethanol. Only a small amount of precipitate was formed in the bromination reaction. This, and the fact that 7 atoms of bromine are consumed in the 2,3-tetramethyl indolene reaction as compared to 8 atoms of bromine in the bromination of 2-phenylaminotetramethyl ethanol, proves that the two reactions are of a distinctly different type. In the case of the bromination test on the indolene the end point obtained in the sodium thiosulfate titration shifted very badly and really never reached a definite constant value. This suggests that the increased tendency for the end point to shift in the bromination of the more highly rearranged samples of 2-phenylaminotetramethyl ethanol, may have been due to small quantities of 2,3-tetramethyl indolene formed under the conditions of the rearrangement. Since the indolene is not brominated in the same manner as the amino alcohol, and since the rates of rearrange-

ment showed no tendency to deviate from constant values, the indolene reaction could not have been of major importance.

The residue obtained from the fractionation of the 2,3-tetramethyl indolene was a very sticky brown gum. It boiled at 220° under a pressure of 0.5 mm. of mercury. It was insoluble in water and in dilute hydrochloric acid but was sparingly soluble in concentrated hydrochloric acid. It was soluble in methyl iodide and upon evaporation of the solvent a brittle substance was obtained, whereas other solvents such as benzene, ether and ligroin gave back the original sticky mass. Refluxing 24 hours with acetyl chloride caused no apparent change. These results indicated that the compound was N-diphenyl-2,3,5,6-octamethyl piperazine formed through the condensation of two molecules of aniline with two molecules of pinacol chlorohydrine.

Analysis (Pregel). Calc for $C_{24}H_{34}N_2$; C, 82.23, H, 9.76; N, 7.99. Found: C, 80.03, 80.24; H, 9.12, 9.30; N, 9.36, 9.62. Molecular weight (cryoscopic benzene) 320 as compared to the theoretical 338.2.

These condensation reactions with the formation of 2,3-tetramethyl indolene and N-diphenyl-2,3,5,6-octamethyl piperazine, resemble the results of Rindfusy and Harnack²⁴ who obtained indolene and n-diphenyl piperazine upon condensation of β -hydroxyethyl-aniline by means of phosphorus pentoxide. However, they found that the piperazine formed readily, but were able to obtain only small quantities of the indolene; whereas we obtained more of the indolene than of the piperazine.

²⁴Rindfusy and Harnack, J. Am. Chem. Soc., 42, 1720 (1920).

SUMMARY

1. The Stieglitz theory of the pinacol-pinacolone and amino alcohol rearrangements has been presented.
2. 2-Phenylaminotetramethyl ethanol has been prepared from pinacol oxide and sodium anilide. This is a new compound and the method of preparation is a new one for the preparation of a 2-amino alcohol. The 2-phenylaminotetramethyl ethanol hydrochloride has also been prepared.
3. Upon bromination, 2-phenylaminotetramethyl ethanol was found to be oxidized to tribromoaniline and two molecules of acetone. This is a new type of reaction for the 2-phenylamino alcohols. The reaction consumes 8 atoms of bromine, whereas aniline requires 6 atoms of bromine for its bromination. These facts are applied in a method of analysis of mixtures of 2-phenylaminotetramethyl ethanol and aniline and this bromination method was used to determine the rates of rearrangement of 2-phenylaminotetramethyl ethanol.
4. The ionization constant of 2-phenylaminotetramethyl ethanol was determined from the hydrogen ion concentrations of solutions of the hydrochloride, and was found to be $K_I = 2.70 \times 10^{-8}$.
5. 2-Phenylaminotetramethyl ethanol does not rearrange when heated alone at 175° for 74 hours.
6. 2-Phenylaminotetramethyl ethanol does rearrange in the presence of water when heated at 175° for 25 hours.
7. The rearrangement of aqueous solutions of 2-phenylaminotetramethyl ethanol hydrochloride takes place readily at 130° . The reaction is monomolecular.
8. The rate of rearrangement of 2-phenylaminotetramethyl ethanol hydrochloride is not greatly increased by the presence of hydrochloric acid in excess of the amount required for complete formation of the hydrochloride. This fact is in marked contrast to the decided increase in the rate of rearrangement of 2-aminotetramethyl ethanol (at 175°) in the presence of excess acid; it shows that the supplementary tendency of the pinacol group to promote the rearrangement has almost been eliminated in the case of the 2-phenylaminotetramethyl

ethanol, as a consequence of its lower temperature of rearrangement (130°).

9. Thus, the character of the rearrangement of 2-phenylaminotetramethyl ethanol is in good agreement with the Stieglitz theory of the rearrangement of strongly basic amino alcohols.
10. 2,3-Tetramethyl indolene has been prepared by the action of pinacol chlorohydrine on aniline. It has been shown that the formation of this indolene does not take place to more than a negligible extent under the conditions of rearrangement of 2-phenylaminotetramethyl ethanol.

